

REMARKS/ARGUMENTS

Claims 25-38 and 50-68 are active in the present application. The claims have been amended to correct typographical errors. No new matter is added. Favorable reconsideration is requested.

Claims 25-32, 35-38, 50-58 and 63-68 are rejected under 35 U.S.C. § 103(a) over either Kornfeld (AY-2 or AZ-2) or Cuozzo in view of Bao et al (U); Claims 39-42 and 47-49 are rejected under 35 U.S.C. § 103(a) over either Kornfeld (BW); and Claims 69-72 are rejected under 35 U.S.C. § 103(a) over either Kornfeld (BW) in view of Bao et al (U). These rejections are traversed for the following reasons.

The present claims provide methods of modifying a lysosomal hydrolase with, for example, N-acetylglucosamine-1-phosphotransferase with a specific activity of at least  $10^6$  pmol/h/mg, e.g., see Claim 25 and modifying a lysosomal hydrolase with phosphodiester  $\alpha$ -GlcNAcase with a specific activity of at least about 472,000 units/mg, e.g., see Claim 39.

The primary point of contention in this application is whether the references cited in the Official Action, in fact, enable one of skill in the art to purify the enzymes to the purities claimed herein. As discussed in great detail in Applicant's previous response, prior to the present invention, there was no disclosure or teaching that directed and enabled one to obtain and isolate either the phosphodiester  $\alpha$ -GlcNAcase or phosphodiester  $\alpha$ -GlcNAcase, which modify the oligosaccharide structure of lysosomal glycoproteins, which in turn, enables the efficient delivery of lysosomal enzymes to the lysosome.

In the outstanding Office Action, the Office maintained the rejection based on the incorrect presumption that one, with the cited references, could have purified the enzymes "to the claimed purity using this reference, absent very convincing proof to the contrary." (see, e.g., page 3 of the Official Action, emphasis in the original).

First, Applicant directs the Examiner's attention to the discussion of enablement in M.P.E.P § 2121.02: "A REFERENCE DOES NOT CONTAIN AN "ENABLING DISCLOSURE" IF ATTEMPTS AT MAKING THE COMPOUND OR COMPOSITION WERE UNSUCCESSFUL BEFORE THE DATE OF INVENTION."

Attached hereto is a Declaration under 37 C.F.R. 1.132 from the Applicant of this application, Dr. William M. Canfield, who attests to the difficulty in purifying the enzymes to high purity prior to the present invention as well as the undue experimentation it would require to again isolate the antibodies used for the purification procedure (see paragraph 6 of the Declaration). Furthermore, Dr. Canfield states the antibody properties useful for purification and the difficulty in isolating similar or the same antibodies once again (see paragraph 7 of the Declaration).

As discussed at length previously, it is clear that the combination of prior art does not enable the purification of the phosphotransferase or phosphodiester  $\alpha$ -GlcNacase with the specific activity in the present claims (see 37 C.F.R. § 1.801-1.809 and MPEP, Chapter 2400). Therefore, the present claims would not have been obvious in view of the cited prior art and as such withdrawal of the rejections under 35 U.S.C. § 103(a) is requested.

The rejections under 35 U.S.C. § 112, second paragraph are addressed by amendment.

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Applicant submits that the present application is ready for allowance. Early notification of such allowance is requested.

Respectfully submitted,

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